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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,962	01/09/2001	Simon Santa-Cruz	00801.0192.NPUS00	9671

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 02/26/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/758,962

Applicant(s)

SANTA-CRUZ ET AL.

Examiner

Celine X Qian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) 32-37 and 39-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 and 38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-52 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group I in Paper No. 14 is acknowledged.

Applicants further elected IRES sequence listed in SEQ ID NO:1, and the corresponding polynucleotide of claim 38. The election of one nucleotide is a restriction requirement instead of a species election.

Accordingly, claims 32-37 and 39-52 are withdrawn from examination for being directed to non elected subject matter. Claims 1-31 and 38 are currently under examination.

Claim Objections

Claim 4 is objected to for containing non-elected subject matter. The claims encompass SEQ ID NO: 1-7. Applicants elected SEQ ID NO: 1. Amending the claims such that they are only directed to elected inventions is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Claim 38 is directed to a plasmid constructs pIRESs-XCP. Applicants disclose that a biological deposit is made with this plasmid. The deposit rules (37 CFR 1.801 - 1.809) set forth examining procedures and conditions of deposit which must be satisfied when a deposit is made (See MPEP 2402-2404). The information disclosed by the instant specification (on page 12) does not meet the rule regarding biological deposit. The following is the guidelines for complete information regarding biological deposit.

Complete information should include a declaration by applicant, assignee, or applicant's agent identifying a deposit of biological material and averring the following (see 37 CFR 1.801 through 1.809):

1) Identifies declarant.

2) States that a deposit of the material has been made in a depository affording permanence of the deposit and ready accessibility thereto by the public if a patent is granted. The depository is to be identified by name and address.

3) States that the deposited material has been accorded a specific accession number.

4) States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent.

5) States the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 U.S.C. § 122.

6) States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least

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thirty years after the date of deposit or for the enforceable life of the patent, whichever period longer.

7) That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent. Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, date of deposit, name and address of the depository, and the complete taxonomic description.

Claim 18 is drawn to a potato virus X viral vector comprising a viral genome, an IRES sequence and virus coat protein gene, wherein the PVX based vector gives rise to single cell infection sites. However, the specification discloses that single cell infection sites result from the infection of a viral construct comprising GFP and CP genes with IRES completely deleted (see page 21, bottom line). Infection of leaves with viral constructs comprising GFP, IRES and CP demonstrates cell-to-cell movement, thus produces large lesions (see Table 3 and page 20, lines

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16-24). The prior art does not teach infection of leaves with such a construct comprising GFP, IRES and CP would result in single cell infection sites either. Santa Cruz et al. teach that CP protein is required for cell-to-cell movement (page 6288, 1st col., lines 4-5) and infection of PVX without CP gene results in single cell infection sites (see Figure 2C and page 6289, 1st col., 2nd col., lines 1-9). In view of the teaching of the specification and art, one skilled in the art would have to engage in undue experimentation to make and use such construct as claimed.

Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: “*specification* shall contain a written description of the invention. . . [emphasis added].” The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that “as of the filing date sought, [the inventor] was in possession of the invention.” See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in “possession” of the invention claimed by describing the invention with all of its claimed limitations “by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention.” See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

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The claims encompass any naturally occurring IRES, fragment of said IRES (claim 3) and a fragment of SEQ ID NO:1 (claim 4). The specification only disclose an IRES isolated from Tobamovirus that can direct translation *in vitro*. The specification does not disclose any other naturally occurring IRES that can direct translation *in vitro*. Moreover, the specification fails to disclose any specific fragment(s) of said Tobamovirus IRES that is able to direct translation *in vitro*. It is unclear what is the size and which part of the Tobamovirus IRES (SEQ ID NO:1) sequence is necessary for its function. Thus, the structure function relationship of the IRES is missing. The specification neither describes a representative number of species by their complete structure nor other relevant identifying characteristics. Therefore, the specification fails to describe the invention in such a way to reasonably convey one skilled in the art that the inventors had possession of the invention at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, 7, 14, 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 2-5 and 7, the recitation of “promoter 5’ to (1), (2) and (3) transcribes a mRNA” renders the claim indefinite because the promoter does not transcribe mRNA. In addition, the promoter can only be 5’ to a nucleic acid sequence, not a number such as (1), (2) or (3).

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Regarding claims 26-28, the word "derived" renders the claims indefinite because the number and nature of the derivative process is unknown.

Claim 14 recites the limitation "reporter gene" in line 1. There is insufficient antecedent basis for this limitation in the claim. Neither claim 12 or 13 has this limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 9-11 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Ivanov et al. (1997, Virology, Vol 232, 32-43).

Ivanov et al. disclose an IRES isolated from Tobamovirus (crTMV) genome, IRES_{cp} (see page 40, 2nd col., 3rd paragraph, lines 1-7, also figure 6). Ivanov et al. also disclose a vector, pHΔβNPTCP, which comprising a T7 promoter, inverted tandem repeat, β-sequence of potato virus X, a nucleic acid encoding neomycin phosphotransferase I gene, the IRES_{cp}, and the Coat protein (CP) gene of the crTMV (see page 33, 2nd col., 4th paragraph, lines 3-14, and Figure 4). Ivanov et al. also disclose a vector comprising a stable stem loop structure 5' to the IRES, wherein this structure blocked the expression of CP protein expression (see page 39, 1st col., lines 1-4, and Figure 7 A, B, C). Therefore, Ivanov et al. disclose the instantly claimed inventions.

Claim 30 is rejected under 35 U.S.C. 102(b) as being anticipated by Martinez-Salas et al (1993, J. Virology, Vol. 67, No. 7, pp. 3748-3755).

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Martinez-Salas et al. disclose a single nucleotide substitution in the IRES of foot-mouth disease virus leads to enhanced translation *in vivo* (See title and Abstract). Therefore, Martinez-Salas et al. disclose the instantly claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-8, 12-17, 19-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Santa Cruz et al. (1996, PNAS, Vol 93, pp. 6286-6290), in view of Ivanov et al.

Santa Cruz et al. teach a potato virus X (PVX) based viral vector comprising a green fluorescent protein (GFP) gene linked to CP of the PVX by FMDV 2A peptide (see page 6287, 2nd col., 3rd paragraph). Santa Cruz et al. teach that the FMDV 2A peptide can direct cleavage of the fusion product which would result a GFP and a CP (see page 6287, 2nd col., 4th paragraph).

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Santa Cruz et al. further teach that this post translational cleavage of polyprotein can be incomplete resulting accumulation of a GFP-2A-CP fusion protein, a GFP-2A fusion protein and PVX CP lacking the first 3 amino acid (see page 6287, 2nd col., 5th paragraph, last two lines). However, Santa Cruz et al. do not teach such a vector comprising an IRES in between these two genes. Santa Cruz et al. do not teach a vector comprising an IRES and stem loop structure upstream or downstream of said structure.

The teaching of Ivanov et al. is discussed above.

It would have been obvious to one of ordinary skill in the art to construct a PVX based viral vector comprising GFP, IRES and CP gene based on the combination teaching of Santa Cruz et al. and Ivanov et al. The ordinary artisan would have been motivated to do so because the IRES would increase the expression of the second protein, CP, thus a better strategy for expressing both free GFP and CP than using FMDV 2A peptide. The level of skill in the molecular cloning is high. Absent evidence to the contrary, one of ordinary skill of art would have reasonable expectation of success to insert the IRES taught by Ivanov in between GFP and CP in the PVX based construct. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill of art at the time the invention was made.

It would also have been obvious to one of ordinary skill in the art to construct a PVX based viral vector comprising GFP, IRES and CP gene with stem loop structure upstream or downstream the IRES based on the teaching of Ivanov et al. and Santa Cruz et al. Ivanov et al. teach a vector comprising (5' to 3') stem loop structure, CP gene, IRES and GUS gene, wherein the presence of the stem loop structure prevents CP gene expression only but not GUS in the presence of IRES immediately upstream of GUS. Base on this teaching, one of ordinary skill in

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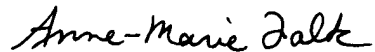
the art would be motivated to make a construct having stem loop structure either upstream or downstream of the IRES to test whether the IRES is efficient in translation initiation. The level of skill in the art of molecular cloning is high, and inserting a sequence comprising a stem loop structure in a vector at any place is routine experimentation. Absent evidence to the contrary, one of ordinary skill in the art would have reasonable expectation of success to make constructs comprising GFP, IRES and CP gene with stem loop structure upstream or downstream of IRES. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
February 22, 2003


ANNE-MARIE FALK, PH.D.
PRIMARY EXAMINER